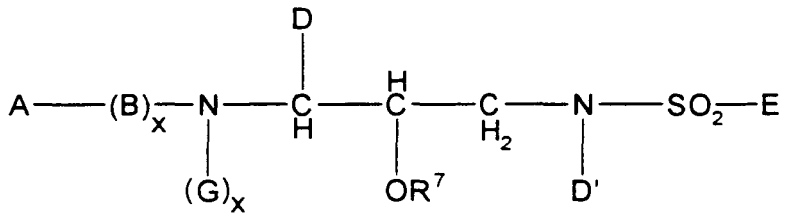
Claims

We claim:

1. A compound of formula (I):



(I)

wherein:

A is selected from H; Ht; $-R^1$-Ht; $-R^1-C_1-C_6$ alkyl, which is optionally substituted with one or more groups independently selected from hydroxy, C_1-C_4 alkoxy, Ht, -O-Ht, $-NR^2-CO-N(R^2)_2$ or $-CO-N(R^2)_2$; $-R^1-C_2-C_6$ alkenyl, which is optionally substituted with one or more groups independently selected from hydroxy, C_1-C_4 alkoxy, Ht, -O-Ht, $-NR^2-CO-N(R^2)_2$ or $-CO-N(R^2)_2$; or R^7;

each R^1 is independently selected from $-C(O)-$, $-S(O)_2-$, $-C(O)-C(O)-$, $-O-C(O)-$, $-O-S(O)_2$, $-NR^2-S(O)_2-$, $-NR^2-C(O)-$ or $-NR^2-C(O)-C(O)-$;

each Ht is independently selected from C_3-C_7 cycloalkyl; C_5-C_7 cycloalkenyl; C_6-C_{10} aryl; or a 5-7 membered saturated or unsaturated heterocycle, containing one or more heteroatoms selected from N, $N(R^2)$, O, S and $S(O)_n$; wherein said aryl or said heterocycle is optionally fused to Q; and wherein any member of said Ht is optionally substituted with one or more substituents independently selected from oxo, $-OR^2$, SR^2, $-R^2$, $-N(R^2)(R^2)$, $-R^2-OH$, -CN, $-CO_2R^2$, $-C(O)-N(R^2)_2$, $-S(O)_2-N(R^2)_2$, $-N(R^2)-C(O)-R^2$, $-C(O)-R^2$, $-S(O)_n-R^2$, $-OCF_3$, $-S(O)_n-Q$, methylenedioxy, $-N(R^2)-S(O)_2(R^2)$, halo, $-CF_3$, $-NO_2$, Q, -OQ, $-OR^7$, $-SR^7$, $-R^7$, $-N(R^2)(R^7)$ or $-N(R^7)_2$;

each R^2 is independently selected from H, Ht or C_1-C_6 alkyl optionally substituted with Q or R^{10};

B, when present, is $-N(R^2)-C(R^3)_2-C(O)-$;

each x is independently 0 or 1;

each R^3 is independently selected from H, Ht, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_3-C_6 cycloalkyl or C_5-C_6 cycloalkenyl; wherein any member of said R^3, except H, is optionally substituted with one or more substituents selected from $-OR^2$, $-C(O)-NH-R^2$, $-S(O)_n-N(R^2)(R^2)$, Ht, $-CN$, $-SR^2$, $-CO_2R^2$, $NR^2-C(O)-R^2$;

each n is independently 1 or 2;

G, when present, is selected from H, R^7 or C_1-C_4 alkyl, or, when G is C_1-C_4 alkyl, G and R^7 are bound to one another either directly or through a C_1-C_3 linker to form a heterocyclic ring; or

when G is not present, the nitrogen to which G is attached is bound directly to the R^7 group in $-OR^7$ with the concomitant displacement of one -ZM group from R^7;

D is selected from Q; C_1-C_6 alkyl or C_2-C_4 alkenyl, which is optionally substituted with one or more groups selected from C_3-C_6 cycloalkyl, $-OR^2$, -S-Ht, $-R^3$, -O-Q or Q; C_3-C_6 cycloalkyl or C_5-C_6 cycloalkenyl, which is optionally substituted with or fused to Q;

each Q is independently selected from a 3-7 membered saturated, partially saturated or unsaturated carbocyclic ring system; or a 5-7 membered saturated, partially saturated or unsaturated heterocyclic ring containing one or more heteroatoms selected from O, N, S, $S(O)_n$ or $N(R^2)$; wherein Q is optionally substituted with one or more groups selected from oxo, $-OR^2$, $-R^2$, $-N(R^2)_2$, $-N(R^2)-C(O)-R^2$, $-R^2-OH$, $-CN$, $-CO_2R^2$, $-C(O)-N(R^2)_2$, halo or $-CF_3$;

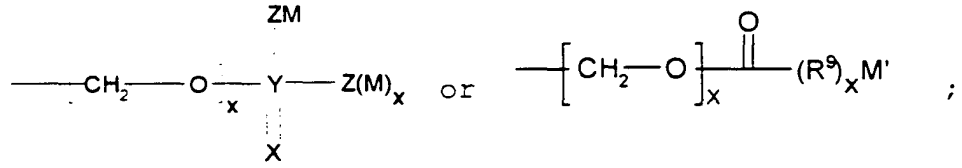
D' is selected from $-OR^{10}$, $-N=R^{10}$ or $-N(R^{10})-R^1-R^3$;

E is selected from Ht; O-Ht; Ht-Ht; $-O-R^3$;

$-N(R^2)(R^3)$; C_1-C_6 alkyl, which is optionally substituted with one or more groups selected from R^4 or Ht; C_2-C_6 alkenyl, which is optionally substituted with one or more groups selected from R^4 or Ht; C_3-C_6 saturated carbocycle, which is optionally substituted with one or more groups selected from R^4 or Ht; or C_5-C_6 unsaturated carbocycle, which is optionally substituted with one or more groups selected from R^4 or Ht;

each R^4 is independently selected from $-OR^2$, $-SR^2$, $-C(O)-NHR^2$, $-S(O)_2-NHR^2$, halo, $-NR^2-C(O)-R^2$, $-N(R^2)_2$ or $-CN$;

each R^5 is independently selected from hydrogen,



; wherein each M is independently selected from H, Li, Na, K, Mg, Ca, Ba, $-N(R^2)_4$, C_1-C_{12}-alkyl, C_2-C_{12}-alkenyl, or $-R^6$; wherein 1 to 4 $-CH_2$ radicals of the alkyl or alkenyl group, other than the $-CH_2$ that is bound to Z, is optionally replaced by a heteroatom group selected from O, S, S(O), $S(O_2)$, or $N(R^2)$; and wherein any hydrogen in said alkyl, alkenyl or R^6 is optionally replaced with a substituent selected from oxo, $-OR^2$, $-R^2$, $N(R^2)_2$, $N(R^2)_3$, R^2OH, $-CN$, $-CO_2R^2$, $-C(O)-N(R^2)_2$, $S(O)_2-N(R^2)_2$, $N(R^2)-C(O)-R^2$, $C(O)R^2$, $-S(O)_2-R^2$, OCF_3, $-S(O)_2-R^6$, $N(R^2)-S(O)_2(R^2)$, halo, $-CF_3$, or $-NO_2$;

M' is H, C_1-C_{12}-alkyl, C_2-C_{12}-alkenyl, or $-R^6$; wherein 1 to 4 $-CH_2$ radicals of the alkyl or alkenyl group is optionally replaced by a heteroatom group selected from O, S, S(O), $S(O_2)$, or $N(R^2)$; and wherein any hydrogen in said alkyl, alkenyl or R^6 is optionally replaced with a substituent selected from oxo, $-OR^2$, $-R^2$, $-N(R^2)_2$, $N(R^2)_3$, $-R^2OH$, $-CN$, $-CO_2R^2$, $-C(O)-N(R^2)_2$, $-S(O)_2-N(R^2)_2$,

$-N(R^2)-C(O)-R_2$, $-C(O)R^2$, $-S(O)_n-R^2$, $-OCF_3$, $-S(O)_n-R^6$, $-N(R^2)-S(O)_2(R^2)$, halo, $-CF_3$, or $-NO_2$;

Z is O, S, $N(R^2)_2$, or, when M is not present, H.

Y is P or S;

X is O or S;

R^9 is $C(R^2)_2$, O or $N(R^2)$; and wherein when Y is S, Z is not S;

R^6 is a 5-6 membered saturated, partially saturated or unsaturated carbocyclic or heterocyclic ring system, or an 8-10 membered saturated, partially saturated or unsaturated bicyclic ring system; wherein any of said heterocyclic ring systems contains one or more heteroatoms selected from O, N, S, $S(O)_n$ or $N(R^2)$; and wherein any of said ring systems optionally contains 1 to 4 substituents independently selected from OH, C_1-C_4 alkyl, O-C_1-C_4 alkyl or O-C(O)-C_1-C_4 alkyl;

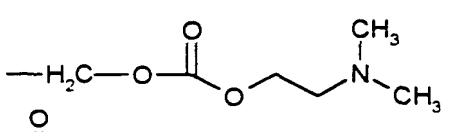
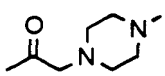
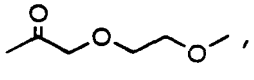
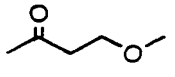
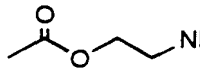
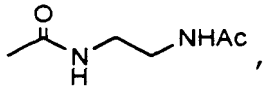
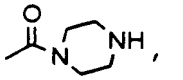
R^8 is selected from C_1-C_8 alkyl, C_3-C_7 alkyl or cyano substituted C_2-C_6 alkenyl; and

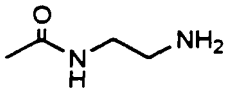
R^{10} is selected from C_1-C_8 alkyl, C_2-C_6 alkenyl, C_6-C_{14} aryl or Ht, wherein R^{10} optionally contains up to three substituents independently selected from $-R^3$, -CN, $-SR^5$, $-SOR^5$, $-SO_2R^5$, $-SR-NR^5-C(O)R^6$, $-NR^5-(SO_2)R^5$, $-C(O)N(R^5)_2$, $-C(S)N(R^5)_2$, $-S(O)_2N(R^5)_2$, $-C(O)R^6$, $-C(S)R^6$, $-N(R^5)_2$, $-NR^5-C(O)R^5$, $-NR^5-C(O)OR^5$, $-NR^5-C(O)N(R^5)_2$, $-NR^5-C(S)R^5$, $-NR^5-C(S)OR^5$, $-NR^5-C(S)N(R^5)_2$, $-NR^5-C[=N(R^5)]-N(R^5)_2$, $-NH-C[=N-NO_2]-NH_2$, $-NH-C[=N-NO_2]-OR^5$, $-N(R^8)_2-C(O)R^8$, $-NH-C[=N-NO_2]-NH_2$, $-NH-C[=N-NO_2]-OR^5$, $-N(R^6)_2-C(O)R^6$, $-OC(O)R^6$, $-OC(O)N(R^5)_2$, $-OC(S)N(R^5)_2$, wherein any one of the $-CH_2$ groups of said alkyl or alkenyl chains of R^{10} may be optionally replaced by O, S, SO, SO_2, C(O) or NR^5;

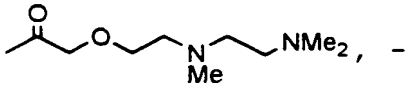
wherein each R^5 is independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl or Ht, wherein each R^5, except for hydrogen, is optionally substituted with -CF3, $-PO_3R^3$, azido or halo;

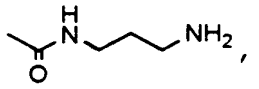
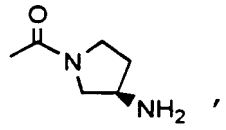
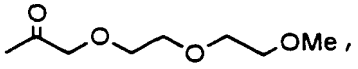
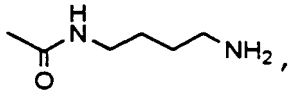
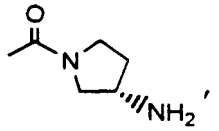
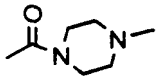
or a pharmaceutically acceptable derivative thereof.

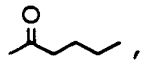
2. The compound according to claim 1, wherein at least one R^7 is selected from:





-(L)-lysine, $-PO_3Na_2$,


-(L)-tyrosine,

$-PO_3Mg$,

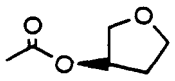
$-PO_3(NH_4)_2$, $-CH_2-OPO_3Na_2$,

-(L)-serine,

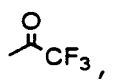
$-SO_3Na_2$,

$-SO_3Mg$, $-SO_3(NH_4)_2$,

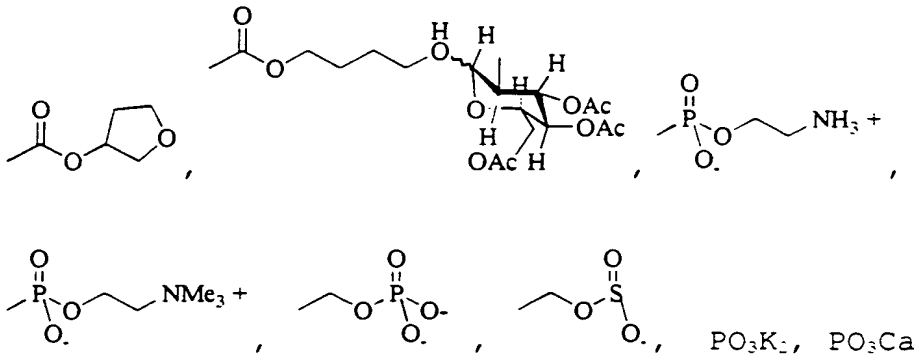
$-CH_2-OSO_3Na_2$, $-CH_2-OSO_3(NH_4)_2$,






acetyl,


-(L)-valine,

-(L)-glutamic acid, -(L)-aspartic acid,

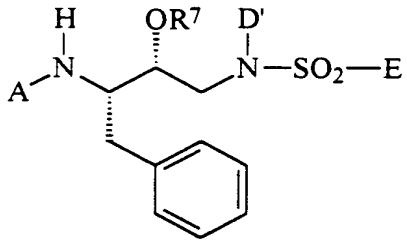
-(L)-γ-t-butyl-aspartic acid,


-(L)-(L)-3-pyridylalanine, -(L)-histidine, -CHO,




PO_3K_2, PO_3Ca, PO_3-spermine, PO_3-(spermidine)$_2$ or PO_3-(meglamine)$_2$.

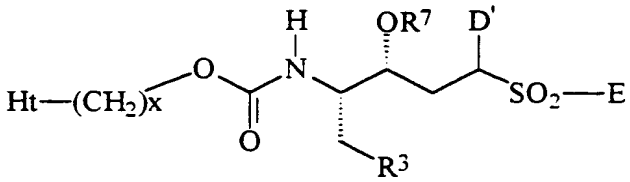
3. A compound of formula (II):



(II)

wherein A, R^7, D' and E are as defined in claim 1;
or a pharmaceutically acceptable derivative thereof.

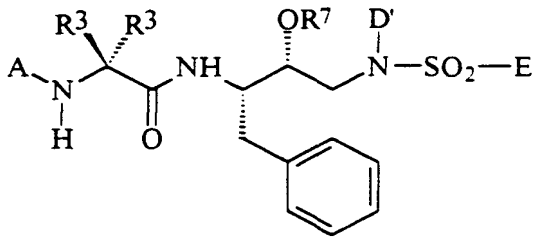
4. A compound of formula (III):



(III)

wherein Ht, x, R^3, R^7, D' and E are as defined in claim 1;
or a pharmaceutically acceptable derivative thereof.

5. A compound of formula (IV):



(IV)

wherein A, R^3, R^7, D' and E are as defined in claim 1; or a pharmaceutically acceptable derivative thereof.

6. The compound according to claim 3, wherein:

A is -C(O)Ht;

D' is $-O-R^{10}$;

E is C_6-C_{10} aryl optionally substituted with one or more substituents selected from oxo, $-OR^2$, SR^2, $-R^2$, $-N(R^2)_2$, $-R^2$-OH, -CN, $-CO_2R^2$, $-C(O)-N(R^2)_2$, $-S(O)_2-N(R^2)_2$, $-N(R^2)-C(O)-R^2$, $-C(O)-R^2$, $-S(O)_n-R^2$, $-OCF_3$, $-S(O)_n$-Q, methylenedioxy, $-N(R^2)-S(O)_2(R^2)$, halo, $-CF_3$, $-NO_2$, Q, -OQ, $-OR^7$, $-SR^7$, $-R^7$, $-N(R^2)(R^7)$ or $-N(R^7)_2$; or a 5-membered heterocyclic ring containing one S and optionally containing N as an additional heteroatom, wherein said heterocyclic ring is optionally substituted with one to two groups independently selected from $-CH_3$, R^4, or Ht.

7. The compound according to claim 3, wherein:

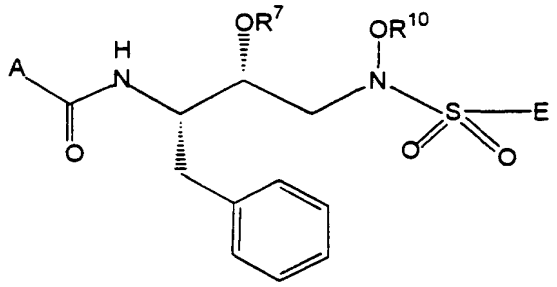
E is a 5-membered heterocyclic ring containing one S and optionally containing N as an additional heteroatom, wherein said heterocyclic ring is optionally substituted with one to two groups independently selected from $-CH_3$, R^4, or Ht.

8. The compound according to claim 3, wherein:

R^7 in $-OR^7$ group shown in formula II is $-PO(OM)_2$ or $C(O)CH_2OCH_2CH_2OCH_2CH_2OCH_3$ and both R^7 in $-N(R^7)_2$ are H; or R^7 in $-OR^7$ group shown in formula II is $C(O)CH_2OCH_2CH_2OCH_3$, one R^7 in $-N(R^7)_2$ is $C(O)CH_2OCH_2CH_2OCH_3$ and the other is H; and

wherein M is H, Li, Na, K or C_1-C_4 alkyl.

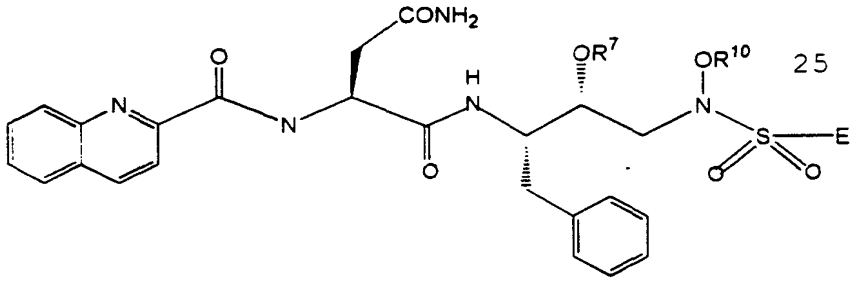
9. A compound according to claim 1, having formula (V):



(V)

wherein A, R^7, R^{10} and E are as defined in claim 1; or a pharmaceutically acceptable derivative thereof.

10. A compound of formula (VI):



(VI)

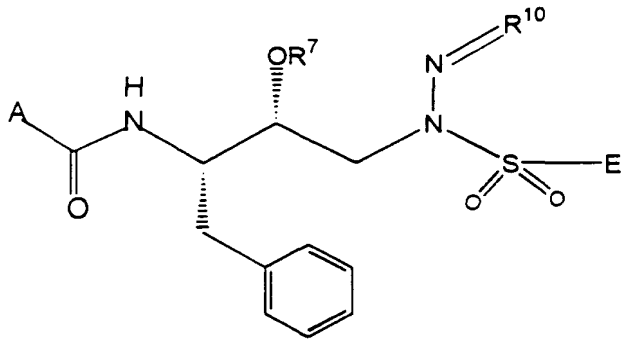
wherein:

R^{10} and R^7 are as defined in claim 1;

E is C_6-C_{14} aryl, optionally substituted with one or more groups selected from the group consisting of nitro, oxo, alkoxy, amino, hydroxyamino; heterocyclcyl, optionally substituted with one or more groups selected from the group consisting of nitro, oxo, alkoxy, amino, hydroxyamino or $N(CO)OCH_3$;

or a pharmaceutically acceptable derivative thereof.

11. A compound of formula (VII):

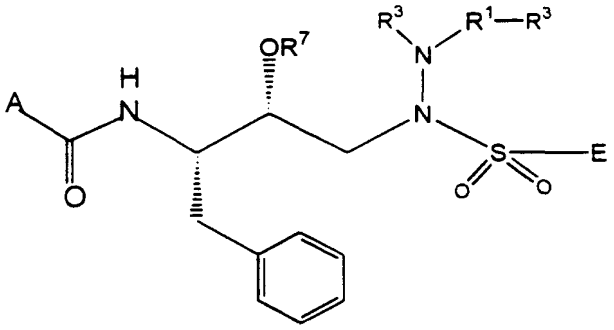


(VII)

wherein A, E, R^7 and R^{10} are as defined in claim 1;

or a pharmaceutically acceptable derivative thereof.

12. A compound of formula (VIII):

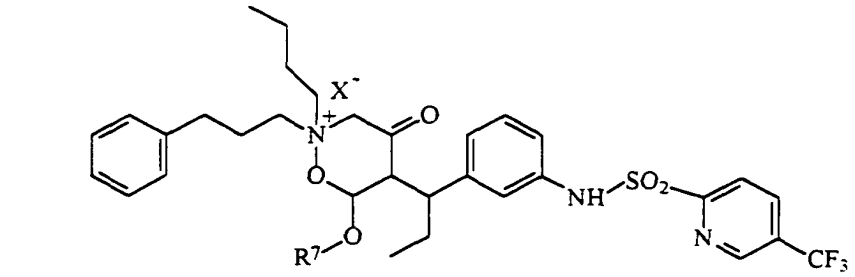


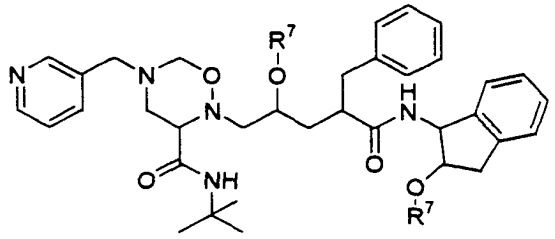
(VIII)

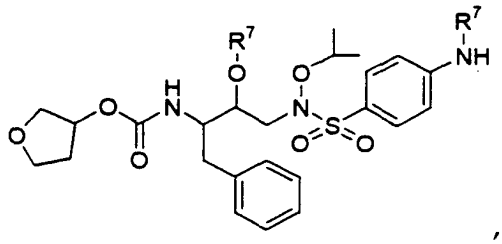
wherein A, R^1, R^3, R^7 and E are as defined in claim 1;

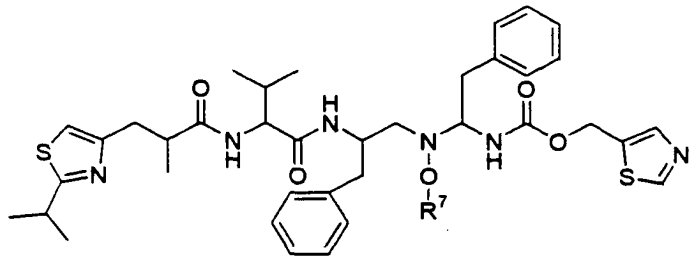
or a pharmaceutically acceptable salt thereof.

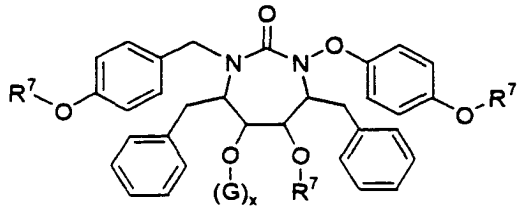
13. A compound selected from:

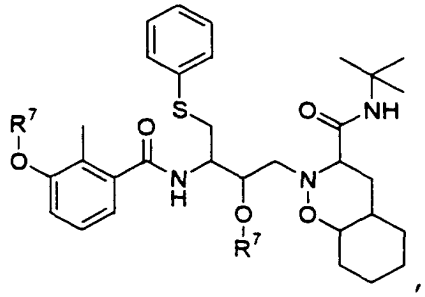


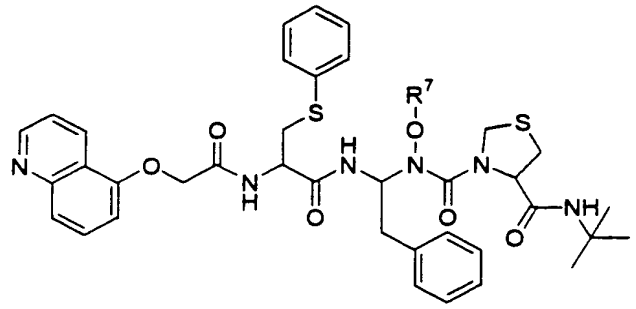


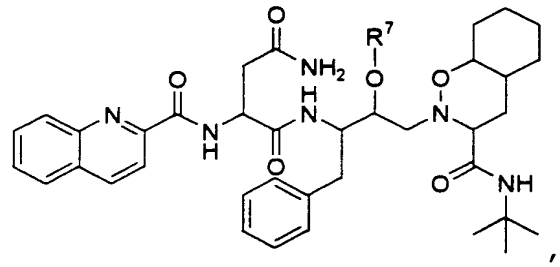


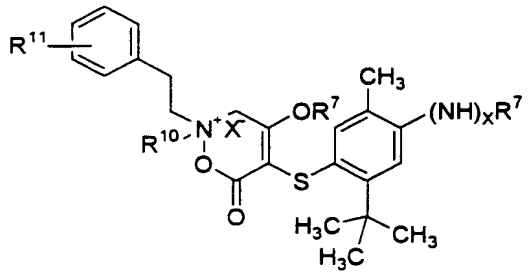












wherein R^{10} is selected from isopropyl or cyclopentyl; R^{11} is selected from NHR^7 or OR^7; x, R^7 and G are as defined in claim 1; and X^- is a pharmaceutically acceptable counterion.

14. A compound selected from:

(3*R*,3a*S*,6a*R*)hexahydrofuro[2,3-*b*]furan-3-yl *N*-((1*S*,2*R*)-1-benzyl-3-(cyclopentyloxy)[(3-[2-(dimethylamino)ethyl]aminophenyl)sulfonyl]amino-2-hydroxypropyl)carbamate;

(3*S*,3a*R*,6a*S*)hexahydrofuro[2,3-*b*]furan-3-yl *N*-((1*S*,2*R*)-1-benzyl-3-(cyclopentyloxy)[(3-[2-(dimethylamino)ethyl]aminophenyl)sulfonyl]amino-2-hydroxypropyl)carbamate;

(3*R*,3a*S*,6a*R*)Hexahydrofuro[2,3-b]furan-3-yl-N-((1*S*,2*R*)-1-benzyl-3-(cyclopentyloxy)(2-[(methylsulfonyl)amino]benzimidazol-5-ylsulfonyl)amino-2-hydroxypropyl)carbamate;

(3*R*,3a*S*,6a*R*)hexahydrofuro[2,3-*b*]furan-3-yl *N*-(1*S*,2*R*)-3-[[(3-N-methylaminophenyl)sulfonyl](cyclopentyloxy)amino]-1-benzyl-2-hydroxypropylcarbamate;

1,3-Dioxan-5-yl N-(1S,2R)-1-benzyl-3-[(cyclopentyloxy)(2-{(methoxycarbonyl)amino]-1H-benzimidazol-5-ylsulfonyl)amino]-2-hydroxypropylcarbamate;

(3*R*,3a*S*,6a*R*)hexahydrofuro[2,3-*b*]furan-3-yl *N*-(1*S*,2*R*)-1-benzyl-2-hydroxy-3-[[(4-methoxyphenyl)sulfonyl](tetrahydro-2*H*-pyran-4-yloxy)amino]propylcarbamate;

(3*R*,3a*S*,6a*R*)hexahydrofuro[2,3-*b*]furan-3-yl *N*-(1*S*,2*R*)-3-[[(3-aminophenyl)sulfonyl](cyclopentyloxy)amino]-1-benzyl-2-hydroxypropylcarbamate;

(3*R*,3a*S*,6a*R*)hexahydrofuro[2,3-*b*]furan-3-yl *N*-[(1*S*,2*R*)-1-benzyl-3-((cyclopentyloxy)[3-(2-[methoxy(methyl)amino]-2-oxoethylamino)phenyl]sulfonylamino)-2-hydroxypropyl]carbamate;

(3*R*,3a*S*,6a*R*)hexahydrofuro[2,3-*b*]furan-3-yl *N*-[(1*S*,2*R*)-1-benzyl-4-(cyclopentyloxy)-2-hydroxy-4-(6-quinoxalinyl sulfonyl)butyl] carbamate;

(3*R*,3a*S*,6a*R*)hexahydrofuro[2,3-*b*]furan-3-yl *N*-((1*S*,2*R*)-1-benzyl-3-(cyclopentyloxy)[(4-methoxyphenyl)sulfonyl]amino-2-hydroxypropyl)carbamate;

(3*R*,3a*S*,6a*R*)hexahydrofuro[2,3-*b*]furan-3-yl *N*-[(1*S*,2*R*)-1-benzyl-3-((cyclopentyloxy)[3-(2-[(methylsulfonyl)amino]ethylamino)phenyl]sulfonylamino)-2-hydroxypropyl]carbamate;

(3*R*,3a*S*,6a*R*)hexahydrofuro[2,3-*b*]furan-3-yl *N*-(1*S*,2*R*)-3-[[(3-N-methylaminophenyl)sulfonyl](cyclopentyloxy)amino]-1-benzyl-2-hydroxypropylcarbamate, phosphate ester;

(3*R*,3a*S*,6a*R*)hexahydrofuro[2,3-*b*]furan-3-yl *N*-(1*S*,2*R*)-3-[[(3-aminophenyl)sulfonyl](cyclopentyloxy)amino]-1-benzyl-2-hydroxypropylcarbamate phosphate ester;

(3R,3aS,6aR) hexahydrofuro [2,3-b]furan-3-yl N-(1S,2R)-3-[[(4-aminophenyl)sulfonyl](cyclopentyloxy)amino]-1-benzyl-2-hydroxypropyl carbamate;

(3R,3aS,6aR)hexahydrofuro[2,3-b]furan-3-yl (1S,2R)-1-benzyl-3-{(1-ethylpropoxy)[(4-hydroxyphenyl)sulfonyl]amino}-2-hydroxypropylcarbamate;

(3R,3aS,6aR)hexahydrofuro[2,3-b]furan-3-yl (1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(1-ethylpropoxy)amino]-1-benzyl-2-hydroxypropylcarbamate;

(3*R*,3a*S*,6a*R*)hexahydrofuro[2,3-*b*]furan-3-yl *N*-[(1*S*,2*R*)-3-[(1,3-benzodioxol-5-ylsulfonyl)(cyclopentyloxy)amino]-1-benzyl-2-(phosphonooxy)propyl]carbamate;

(3*R*,3a*S*,6a*R*)hexahydrofuro[2,3-b]furan-3-yl (1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(cyclohexyloxy)amino]-1-benzyl-2-hydroxypropylcarbamate;

(3*R*,3a*S*,6a*R*)hexahydrofuro[2,3-b]furan-3-yl 3-[(1,3-benzodioxol-5-ylsulfonyl)(tetrahydro-2H-pyran-4-yloxy)amino]-1-benzyl-2-hydroxypropylcarbamate;

(3*R*,3a*S*,6a*R*)hexahydrofuro[2,3-*b*]furan-3-yl *N*-[(1*S*,2*R*)-3-[(1,3-benzodioxol-5-ylsulfonyl)(cyclopentyloxy)amino]-1-benzyl-2-(phosphonooxy)propyl]carbamate;

or a pharmaceutically acceptable derivative thereof.

15. The compound according to claim 1 wherein said compound has a molecular weight less than or equal to about 700 g/mol.

16. The compound according to claim 15 wherein said compound has a molecular weight less than or equal to about 600 g/mol.

17. A pharmaceutical composition comprising an effective antiviral amount of a compound according to any one of claims 1-14 or a pharmaceutically acceptable

derivative thereof together with a pharmaceutically acceptable carrier therefore.

18. The pharmaceutical composition according to claim 17, further comprising an antiviral agent other than a compound according to claims 1-14.

19. A pharmaceutical composition according to claim 17 or 18 in the form of a tablet or capsule.

20. A method of treating a virus infection in a human comprising administering to said human an effective antiviral treatment amount of a compound according to any one of claims 1-13 or a pharmaceutically acceptable derivative thereof.

21. The method according to claim 20 wherein the virus infection is an HIV infection.

22. The method according to claim 20 or 21 wherein said step of administering comprises oral administration or administration by injection.

23. Use of a compound according to any of claims 1-14 for the manufacture of a medicament for the treatment or prophylaxis of a viral infection.

24. Use of a compound according to any of claims 1-14 or a formulation according to claim 17 for use in medical therapy.